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PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) G0744.70042US07

Application Number	Filed
07/839,194-Conf. #6108	February 20, 1992
First Named Inventor: Katherine Gordon et al.	
Art Unit: 1632	Examiner: D. A. Montanari

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant /inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [x] attorney or agent of record. Registration number 36,276
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____

Signature

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April 5, 2010
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of 1 forms are submitted.

Certificate of Electronic Filing Under 37 CFR 1.8

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Dated: April 5, 2010 Signature Eileen Mackenzie

PRE-APPEAL BRIEF REQUEST FOR REVIEW

In response to the Final Office Action dated October 5, 2009, Applicant hereby requests Panel Review of the written description rejections of all the claims (claims 1, 2, 5-8, 11, 16-17 and 30-33) under 35 U.S.C. § 112, first paragraph.[1] The evidence of record shows that the Examiner has failed to make a *prima facie* case so that the rejections are not proper and are without basis. The application describes all mammalian milk promoter sequences, not just the exemplified whey acid protein (WAP) promoter.

The Board reversed the same written description rejection in the corresponding method patent. [Decision mailed July 25, 2003 in 07/938,322.] Moreover, Applicant previously appealed the same rejection in this product application, and the previous Examiner withdrew the rejection for the same reason as the Board reversed the rejections. [Office Action mailed August 7, 2006 at p. 2-3.] The prior actions of the PTO after briefing on appeal, while not determinative, support Applicant's arguments.

When withdrawing the written description rejection regarding "mammalian milk promoter", the previous Examiner introduced a new written description rejection regarding "does not naturally control transcription." [*Id.* at p. 7.] Applicant overcame that rejection, only to have the present Examiner reintroduce the rejection regarding "mammalian milk promoter." [Office Action mailed December 4, 2008 at pp. 2, 3.] The present Examiner's reintroduction of the rejection that Applicants twice overcame on appeal illustrates that reversal of this rejection by the panel would achieve the program's goal of saving resources for Applicant and the PTO. 1296 OG 67 (2005).

The written description rejection of claims 1, 2, 5-8, 11, 16-17 and 30-33 is deficient

The claimed invention is directed to a "DNA construct comprising a gene encoding a promoter, said gene being under transcriptional control of a **mammalian milk protein promoter** . . . ." The Examiner rejected the claims for failing to comply with the written requirement because: 1) the alleged failure to describe a mammalian serum milk protein promoter other than the WAP promoter shows that applicant did not have possession of the invention; 2) the prior art describes only one other milk protein promoter; and 3) one skilled in the art would not have envisioned the

[1] All the claims have also been rejected on the ground of obviousness-type double patenting over US Patent Nos. 6,727,405 and 7,045,676. Applicant will submit terminal disclaimers over those patents upon withdrawal of the written description rejections.

DNA sequence of the encompassed promoters other than the WAP promoter. [Office Action mailed December 4, 2008 at pp. 3-4.] The Examiner did not further support the rejection in the final Office Action but merely responded to Applicant's arguments. [Office Action mailed October 5, 2009 at pp. 2, 4.] The three bases for the rejection are legally and factually deficient.

The evidence shows the application describes promoters other than the WAP promoter

The evidence of record shows that one skilled in the art would have recognized that Applicant had possession of the claimed invention for all mammalian serum milk protein promoters, not just the WAP promoter. First, the application asserts that the claims are described for all mammalian milk promoters, and the Examiner has not provided reasoning or evidence to the contrary. The application discloses that the invention can involve "a mammalian milk protein promoter" [Spec. at p. 2] and includes an entire section on "mammalian milk protein promoters" that can be used in the invention [Spec. at pp. 3-6], including "any promoter naturally associated with any protein which is normally secreted into mammalian milk." [Spec. at pp. 3-4.]

The specification states that other milk protein promoters can be isolated in the same manner as the WAP promoter was isolated, citing to two journal articles. [Spec. at p. 5.] The specification then goes on to describe this known method in detail. [Spec. at pp. 5-6.] Indeed, the specification concludes that milk proteins other than the WAP promoter can be used, including the β-lactoglobulin promoter. [Spec. at p. 15.] Finally, the original claims were not limited to the WAP promoter but recited "a mammalian milk protein promoter." [Spec. at p. 16-18.]

The Examiner has not provided any reason to doubt these statements in the specification, as is required for a *prima facie* rejection. MPEP § 2163 III. A. ("A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption."). The Examiner's mere assertion that the claims are not described for their full scope does not satisfy the Examiner's burden of providing "evidence or reasoning" to challenge "by a preponderance of evidence" the specification's statements. *Id.* The Examiner's failure to establish a *prima facie* case is particularly clear here because there "is a strong presumption" that original claims are adequately described. MPEP § 2163 I. A. Original Claims.

Indeed, the Board reached the same conclusion in the related method patent, holding that similar assertions did not meet "the burden of establishing a *prima facie* case that the specification does not provide an adequate written description of the claimed invention." [Decision at p. 5.]

Second, the prior art of record shows that several mammalian milk protein promoters other than the WAP promoter were in fact known. [*E.g.*, Yu-Lee et al (1983) J Biol Chem 258:10794-10804 (**γ-casein promoter**); Qasaba at al. (1984) Nature 308:377-380 (**α-lactalbumin promoter**); Jones et al. (1985) J Biol Chem 260:7042-7050 (**β-casein promoter**); Yu-Lee et al. (1986) Nucl. Acids Res.14:18834 902 (**α-casein promoter**).] Indeed, the previous Examiner came to the same conclusion in reopening prosecution in the present application after Applicants filed an Appeal Brief. [Office Action mailed August 7, 2006 at p. 3 ("the evidence of record . . . demonstrated that the 5' end of some genes from some species encoding milk proteins were known at the time of filing, and preliminary and routine characterization of said sequences identified transcriptional elements such as the TATA and CAT boxes . . . meeting the requirement of written description.").]

Third, post-filing statements of those skilled in the art demonstrate that Applicant was in possession of the claimed DNA construct for the full scope of "a mammalian milk protein promoter." The experiments reported in the present application were published as a scientific paper in 1987. [Meade Decl. at ¶ 9 (citing Ex. B).] Numerous papers paid tribute to this work as having "started a minirevolution" and having founded an entire industry. [Meade Decl. at ¶ 9 (citing Ex. C-F).] As a result of the 1987 paper, hundreds of lines of transgenic mice, sheep, goats, pigs, and cows that express recombinant proteins in their milk were developed, and several biotechnology companies were formed. [Meade Decl. at ¶ 9 (citing Ex. C, E, G).] Not one of these papers characterized Applicant's invention as limited to the WAP promoter. Rather, they list numerous successes with promoters other than the WAP promoter, and they do not attribute those successes to any intervening developments. [Ex. C at p. 185, Table 1; Ex. D at p. 341, Table I; Ex. E at p. 247, Table 3; Ex. F at p. 2219, Tables 3, 4; Ex. G at p. 133-135, Tables 1-3.] Rather, subsequent knowledge regarding the control of gene expression in the mammary gland "has been of little practical use when it comes to improving transgene expression." [Ex. D at p. 348, col. 2.]

Applicant has supplemented this evidence in the scientific literature with two Declarations. Katherine Gordon, Ph.D. stated:

> Give that . . . the milk proteins coordinately expressed in lactating mammary epithelia were presumed to share similar regulatory mechanisms for expression, one skilled in the art . . . would have reasonably expected that transcriptional regulatory sequences derived from other members of the class of milk serum proteins would function **in the same or similar manner** as the WAP regulatory sequences in the claimed [invention].

[Third Gordon Declaration at ¶. 7 (emphasis added).] Similarly, Harry Meade, Ph.D. stated:

> Because of the seminal work described in the above-referenced patent application, one of ordinary skill in the art was then able to use **milk protein promoters** to express proteins they did not naturally control in the milk of transgenic animals, which, as mentioned above, occurred rapidly after the Gordon et al. 1987 publication.

[Meade Declaration at ¶ 15 (emphasis added).] Thus, the Examiner is clearly incorrect. The application describes promoters other than the WAP promoter.

The sequences of all mammalian milk protein promoters are not required

The Examiner also based the written description rejection on the assertion that the claims require the disclosure of the DNA sequence of mammalian milk protein promoters [Office Action mailed December 4, 2008 at pp. 3-4], and the Examiner has maintained the rejection by relying upon this assertion. [Office Action mailed October 5, 2009 at pp. 9, 10, 11.] Indeed, the Examiner appears to believe the lack of sequences makes Applicant's evidence irrelevant. [*Id* at p. 9 ("evidence is not needed . . . based upon the complete lack of any sequences . . . .").]

"There is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." MPEP § 2163 II. A. 3. (a). (quoting *Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006).] If each of the component DNA sequences of a claim to a DNA sequence is known, as when the invention comprises a new combination of DNA sequences, the known DNA sequences need not be disclosed. *Falkner*, 448 F.3d at 1368 ("[W]e hold that where, as in this case, accessible literature sources clearly provided . . . genes and their nucleotide sequences . . ., satisfaction of the written description requirement does not require [the disclosure] of such genes and sequences."). As discussed above, several mammalian milk promoter sequences were known in the art, and additional such sequences could be, and were, readily obtained. Accordingly, there is no requirement that all such DNA sequences be disclosed in the specification to describe the claims.

Indeed, that is what the Board held in the related method patent:

> We disagree [with the written description rejection.] As appellants explain, there is nothing novel about the individual elements set forth in each claimed step, instead the claim is a novel arrangement of old elements. . . . As we understand appellants' specification, claims, and arguments, a person of ordinary skill in the art need only identify a protein which is normally expressed in milk and use its promoter sequence in the claimed method.

[Decision at pp. 4-5.]

Finally, those skilled in the art expected that mammalian milk promoters other than the WAP promoter would function in the same or a similar manner as the WAP promoter. [Third Gordon Declaration at ¶ 7.] Thus, the disclosure of the WAP (and α-lactalbumin) promoters constitutes a representative number of species that satisfies the written description requirement for the claimed genus. MPEP § 2163 II. A. 3. (a).

The written description rejection of claims 1, 2, 5-8, 11, 16-17 and 30-33 is deficient

Claim 31 faces a related but separate new matter rejection regarding the α-lactalbumin promoter. [Office Action mailed December 4, 2008 at p. 2.] This rejection is inconsistent with the failure to reject claim 17, which also recites an α-lactalbumin promoter. As discussed above, the application does describe an α-lactalbumin promoter.

For the above reasons, the written description rejections are factually and legally deficient. Applicant requests that the application be allowed on the existing claims and prosecution remain closed.

Dated: April 5, 2010

Respectfully submitted,

By _____

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